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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/834,228 | 04/12/2001 | Elaine L. Jacobson | NIAD-214.1 US | 3352 |

24972 7590 06/18/2002
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| EXAMINER |
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HUI, SAN MING R

| ART UNIT | PAPER NUMBER |
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1617
DATE MAILED: 06/18/2002 10

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|--------------------------|------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/834,228 | JACOBSON ET AL. |
| | Examiner San-ming Hui | Art Unit 1617 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on ____.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 17-29 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) Claim(s) ____ is/are allowed.
- 6) Claim(s) 17-29 is/are rejected.
- 7) Claim(s) ____ is/are objected to.
- 8) Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on ____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on ____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. ____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

| | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

The cancellation of claims 1-16 in amendment filed April 1, 2002 is acknowledged. The addition of claims 17-29 in amendment filed April 1, 2002 is acknowledged.

The outstanding rejections of claims 1-7 and 9-16 under 35 USC 112, first and second paragraph is withdrawn in view of the amendment filed April 1, 2002.

Claims 17-29 are pending.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17, 19-22, 24, 25, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Huber (US Patent 2,431,558).

Huber teaches topical administration of 5% of hexyl nicotinate oil lotion to increase the blood flow to tissue (See particularly col. 3, line 17-25; also claims 1-3).

Please note that hexyl nicotinate inherently possesses the log P value recited in claim 1.

Claim Rejections - 35 USC § 103

~ The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 17-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huber (US Patent 2,431,558) in view of Le et al. (International Journal of Pharmaceutics, 1998; 163: 11-22) and Otsuka et al. (US Patent 5,151,271). Le et al. and Otsuka are references of record in the previous office action mailed January 2, 2002.

Huber teaches topical administration of a vasodilator containing composition wherein the vasodilator may be C4-C8 alkyl nicotinate (i.e., butyl, pentyl, hexyl, heptyl, and octyl nicotinate) (See particularly claim 1). Huber also teaches that the topical administration of the alkyl nicotinate may increase the blood flow to tissue (See particularly col. 3, line 43-51). Huber also teaches that the weight percentage of the alkyl nicotinate may be 1-10% (See particularly claim 3).

Huber does not expressly teach the method of topical administration of the alkyl nicotinate composition may enhance the oxygen delivery to tissue. Huber does not expressly teach the alkyl nicotinate having a log P value below 6.0. Huber does not expressly teach the composition comprising butyl benzoate. Huber does not expressly teach the concentration of the active as 0.1% to 1.0%.

Le et al. teaches the P value of octyl niacin is 51182. Therefore the Log P is equal to 4.7 (See page 15, Table 1).

Otsuka et al. teaches that butyl benzoate is useful as an adjuvant agent that indirectly promotes percutaneous absorption of the active in percutaneous application (See particularly col. 4, line 45-57).

 It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate butyl benzoate into the vasodilatation method of Huber. It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate alkyl nicotinate compounds herein in the concentration herein in the method of Huber.

 One of ordinary skill in the art would have motivated to incorporate butyl benzoate into the method of Huber because butyl benzoate is known to be useful as an adjuvant agent that indirectly promotes percutaneous absorption of the active agent. Therefore, incorporate butyl benzoate into the Huber composition would have been reasonably expected to increase the absorption of octyl niacin and thereby increase its vasodilatation activity. Such vasodilatation effect and the increase of blood flow to tissue would therefore be reasonably expected to be effective to increase the delivery of oxygen to tissue. One of ordinary skill in the art would have been motivated to incorporate alkyl nicotinate compounds herein in the concentration herein in the method of Huber because the optimization of result therapeutic parameters (e.g., dosage range) is obvious as being within the skill of the artisan.

Response to Arguments

Applicant's arguments with respect to claims 1-16 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
June 6, 2002

Russell Travers
RUSSELL TRAVERS
PRIMARY EXAMINER
GROUP 1200